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                  data from INPADOC
 NEWS  4  FEB 28  BABS - Current-awareness alerts (SDIs) available
 NEWS  5  MAR 02  GBFULL: New full-text patent database on STN
 NEWS  6  MAR 03  REGISTRY/ZREGISTRY - Sequence annotations enhanced
 NEWS  7  MAR 03  MEDLINE file segment of TOXCENTER reloaded
 NEWS  8  MAR 22  KOREAPAT now updated monthly; patent information enhanced
 NEWS  9  MAR 22  Original IDE display format returns to REGISTRY/ZREGISTRY
 NEWS  10 MAR 22  PATDPASPC - New patent database available
 NEWS  11 MAR 22  REGISTRY/ZREGISTRY enhanced with experimental property tags
 NEWS  12 APR 04  EPFULL enhanced with additional patent information and new
                  fields
 NEWS  13 APR 04  EMBASE - Database reloaded and enhanced
 NEWS  14 APR 18  New CAS Information Use Policies available online
 NEWS  15 APR 25  Patent searching, including current-awareness alerts (SDIs),
                  based on application date in CA/CAplus and USPATFULL/USPAT2
                  may be affected by a change in filing date for U.S.
                  applications.
 NEWS  16 APR 28  Improved searching of U.S. Patent Classifications for
                  U.S. patent records in CA/CAplus
 NEWS  17 MAY 23  GBFULL enhanced with patent drawing images
 NEWS  18 MAY 23  REGISTRY has been enhanced with source information from
                  CHEMCATS
 NEWS  19 JUN 06  The Analysis Edition of STN Express with Discover!
                  (Version 8.0 for Windows) now available
 NEWS  20 JUN 13  RUSSIAPAT: New full-text patent database on STN
 NEWS  21 JUN 13  FRFULL enhanced with patent drawing images
 NEWS  22 JUN 27  MARPAT displays enhanced with expanded G-group definitions
                  and text labels
 NEWS  23 JUL 01  MEDICONF removed from STN
 NEWS  24 JUL 07  STN Patent Forums to be held in July 2005
 NEWS  25 JUL 13  SCISEARCH reloaded

 NEWS EXPRESS  JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

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=> file pctfull

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FULL ESTIMATED COST	0.21	0.21

FILE 'PCTFULL' ENTERED AT 10:47:16 ON 20 JUL 2005

FILE LAST UPDATED: 19 JUL 2005 <20050719/UP>
MOST RECENT UPDATE WEEK: 200528 <200528/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

```
=> s HIP1 or (huntingtin () interacting protein)
            31 HIP1
           405 HUNTINGTIN
             6 HUNTINGTINS
           406 HUNTINGTIN
                 (HUNTINGTIN OR HUNTINGTINS)
         34642 INTERACTING
        122116 PROTEIN
        103067 PROTEINS
        134770 PROTEIN
                 (PROTEIN OR PROTEINS)
          3697 INTERACTING PROTEIN
                 (INTERACTING(W)PROTEIN)
           104 HUNTINGTIN (W) INTERACTING PROTEIN
L1         122 HIP1 OR (HUNTINGTIN (W) INTERACTING PROTEIN)

=> s prostate or colon
         21247 PROSTATE
           381 PROSTATES
         21261 PROSTATE
                 (PROSTATE OR PROSTATES)
         24121 COLON
           508 COLONS
          1601 COLA
         25865 COLON
                 (COLON OR COLONS OR COLA)
L2       34409 PROSTATE OR COLON

=> s l2 and l1
L3          80 L2 AND L1

=> s genes/ti
L4        2913 GENES/TI

=> s l3 and l4
L5           6 L3 AND L4

=> s williams/au
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L6        3387 WILLIAMS/AU

=> s l6 and l5
L7           1 L6 AND L5

=> d ibib

L7     ANSWER 1 OF 1      PCTFULL   COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER:        2000018916 PCTFULL  ED 20020515
TITLE (ENGLISH):         HUMAN GENES AND GENE EXPRESSION PRODUCTS
TITLE (FRENCH):          GENES HUMAINS ET PRODUITS D'EXPRESSION
                         GENIQUE
INVENTOR(S):             WILLIAMS, Lewis, T.;
                         ESCOBEDO, Jaime;
                         INNIS, Michael, A.;
                         GARCIA, Pablo, Dominguez;
                         SUDDUTH-KLINGER, Julie;
                         REINHARD, Christoph;
                         GIESE, Klaus;
                         RANDAZZO, Filippo;
                         KENNEDY, Giulia, C.;
                         POT, David;
                         KASSAM, Altaf;
                         LAMSON, George;
                         DRMANAC, Radoje;
                         CRKVENJAKOV, Radomir;
                         DICKSON, Mark;
                         DRMANAC, Snezana;
                         LABAT, Ivan;
                         LESHKOWITZ, Dena;
                         KITA, David;
                         GARCIA, Veronica;
                         JONES, Lee, William;
                         STACHE-CRAIN, Birgit
PATENT ASSIGNEE(S):      CHIRON CORPORATION;
                         HYSEQ INC.
LANGUAGE OF PUBL.:       English
DOCUMENT TYPE:           Patent
PATENT INFORMATION:
                         NUMBER              KIND     DATE
                         ---------------------------------
                         WO 2000018916         A2 20000406
DESIGNATED STATES
       W:                AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE
                         DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE
                         KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO
                         NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ
                         VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY
                         KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE
                         IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE
                         SN TD TG
APPLICATION INFO.:       WO 1999-US22226       A  19990923
PRIORITY INFO.:          US 1998-60/102,161       19980928
                         US 1998-60/102,180       19980928
                         US 1998-60/102,380       19980929
                         US 1998-60/103,815       19981008
                         US 1998-60/105,877       19981027


=> d kwic

L7     ANSWER 1 OF 1      PCTFULL   COPYRIGHT 2005 Univentio on STN
TIEN   HUMAN GENES AND GENE EXPRESSION PRODUCTS
```

TIFR **GENES** HUMAINS ET PRODUITS D'EXPRESSION GENIQUE

IN **WILLIAMS, Lewis, T.;**
ESCOBEDO, Jaime;
INNIS, Michael, A.;
GARCIA, Pablo, Dominguez;
SUDDUTH-KLINGER, Julie;
REINHARD, Christoph;
GIESE, Klaus;
RANDAZZO, Filippo;
KENNEDY, Giulia, C.;
POT, David;
KASSAM, Altaf;
LAMSON, George;
DRMANAC, Radoje;
CRKVENJAKOV, Radomir;
DICKSON, Mark;
DRMANAC, Snezana;
LABAT,. . .

DETD The invention features polynucleotides that are expressed in human tissue, specifically
human **colon**, breast, and/or lung tissue. Novel nucleic acid compositions of the invention of
particular interest comprise a sequence set forth in any. . .
. . .
generating the cDNA. Where the provided
I 0 polynucleotides are isolated from cDNA libraries, the libraries are prepared from mRNA of human
colon cells, more preferably, human **colon** cancer
cells., even more preferably, from a highly
metastatic **colon** cell, Km 12L4-A.
. . .
sample, or any normal
tissue of the patient, especially those that express the
poiynucleotide-related gene of interest (e.g.,
brain, thymus, testis, heart, **prostate**, placenta, spleen,
small intestine, skeletal muscle, pancreas, and
the mucosal lining of the **colon**). A difference between the
polynucleotide-related gene, mRNA, or
protein in the two tissues which are compared, for example in molecular weight,. . .
. . .
a test sample obtained from a patient suspected of having or being susceptible to a disease
(e.g., breast cancer, lung cancer, **colon** cancer and/or
metastatic forms thereof), and comparing the
detected levels to those levels found in non-nal cells (e.g., cells substantially unaffected. . .
. . .
of breast cancer), lung cancer
(e.g., small cell carcinoma, non-small cell carcinoma, mesothelioma, and other forms and/or stages of
lung cancer), and **colon** cancer (e.g., adenomatous polyp,
colorectal carcinoma, and other forms
and/or stages of **colon** cancer).
. . .
polynucleotide is differentially expressed across various cancer types. Thus,
for example, expression of a polymicleotide that has clinical implications for metastatic **colon** cancer
can also have clinical implications for stomach cancer or endometrial cancer.

Detection of **colon** cancer. The polynucieotides of the invention exhibiting the appropriate expression pattern can be used to detect **colon** cancer in a subject. Colorectal cancer is one of the 1 5 most common neoplasms in humans and perhaps the most. . . . colorectal cancer. Colorectal cancer begins as polyps, which are small, benign growths of cells that form on the inner lining of the **colon**. Over a period of several years, some of these polyps accumulate additional mutations and become cancerous. Multiple familial colorectal cancer disorders have been identified, which are summarized as follows: 1) Familial adenomatous polyposis (FAP); 2) Gardner's syndrome; 3) Hereditary nonpolyposis **colon** cancer (HNPCC),- and 4) Familial colorectal cancer in Ashkenazi Jews. The expression of appropriate polynucleotides of the invention can be used in the diagnosis, prognosis and management of colorectai cancer. Detection of **colon** cancer can be determined using expression levels of any of these sequences alone or in combination with the levels of expression.

Determination of the aggressive nature and/or the metastatic potential of a **colon** cancer can be determined by comparing levels of one or more polynucleotides of the invention and comparing total levels of another sequence. . . Nat Genet. (I 994) 4(3):217; Fearon ER, Ann N YAcad Sci. (I 995) 768: 1 0 1). For example, development of **colon** cancer can be detected by examining the ratio of any of the polynucleotides of the invention to the levels of oncogenes. . .

FAP or p53). Thus expression of specific marker polynucleotides can be used to discriminate between normal and cancerous **colon** tissue, to discriminate between **colon** cancers with different cells of origin, to discriminate between **colon** cancers with different potential metastatic rates, etc.

3 5 Detection of **prostate** cancer. The polynucleotides and their corresponding genes and gene 3 8 products exhibiting the appropriate differential expression pattern can be used to detect **prostate** cancer in a subject. Over 95% of primary **prostate** cancers are adenocarcinomas. Signs and symptoms may include: frequent urination, especially at night, inability to urinate, trouble starting or holding back urination,. . .

Many of the signs and symptoms of **prostate** cancer can be caused by a variety of other non-cancerous conditions. For example, one common cause of many of these signs and symptoms is a condition called benign prostatic hypertrophy, or BPH. In BPH, the **prostate** gets bigger and may block the flow or urine or interfere with sexual function. The methods and compositions of the invention can be used to distinguish between **prostate** cancer and such non-cancerous conditions.

invention can be used in conjunction with conventional methods of diagnosis,
e.g., digital rectal exam and/or detection of the level of **prostate** specific antigen (PSA), a substance
produced and secreted by the **prostate**.

1: Source of Biological Materials and Overview of Novel Polynucleotides Expressed b
the Biological Materials
cDNA libraries were constructed from either human **colon** cancer cell line Km 12L4-A
(Morikawa, et al., CancerResearch (1988) 48:6863), KM12C (Morikawa et al. CancerRes. (1988)
48:1943-1948), or MDA-MB-231 (Brinkley et. . .

2L49 KM I 2L4-A. etc.) are wel 1-recognized in the art as a model cell line for the study of **colon**
cancer (see, e.g., Moriakawa et aL, supra; Radinsky et aL Clin. Cancer Res. (I 995) 1:19; Yeatman et
I 0 aL, (I. . .

56
Table 4. Description of cDNA Libraries
Library Description Number of
(lib Clones in
Library
I Human **Colon** Cell Line Km 12 L4: High Metastatic 308731
Potential (derived from Km 12C)
2 Human **Colon** Cell Line Km 12C: Low Metastatic 284771
Potential
3 Human Breast Cancer Cell Line MDA-MB-23 1: High 326937
Metastatic Potential; micro-mets in lung
4. . . bFGF 42100
TREATED (PCR (OligodT) cDNA library)
14 Human microvascular endothelial cells (HMVEQ - 42825
VEGF TREATED (PCR (OligodT) cDNA library)
1 5 Normal **Colon** - UC#2 Patient (MICRODISSECTED PCR 282722
(OligodT) cDNA library)
16 **Colon** Tumor - UC#2 Patient (MICRODISSECTED PCR 298831
(OligodT) cDNA library)
1 7 Liver Metastasis from **Colon** Tumor of UC#2 Patient 303467
(MICRODISSECTED PCR (OligodT) cDNA library)
18 Normal **Colon** - UC#3 Patient (MICRODISSECTED PCR 36216
(OligodT) cDNA library)
19 **Colon** Tumor - UC#3 Patient (MICRODISSECTED PCR 41388
(OligodT) cDNA library)
20 Liver Metastasis from **Colon** Tumor of UC#3 Patient 30956
(MICRODISSECTED PCR (OligodT) cDNA library)
21 GRRpz Cells derived from normal **prostate** epithelium 164801
22 WOca Cells derived from Gleason Grade 4 **prostate** 162088
cancer epithelium
23 Normal Lung Epithelium of Patient # 1 006 306198
(MICRODISSECTED PCR (OligodT) cDNA library)
Primary tumor, Large Cell Carcinoma of. . .

Donna M. Peehl, Department of Medicine, Stanford University School of Medicine. GRRpz was
derived from normal **prostate** epithelium. The WOca cell line is a Gleason Grade 4 cell line.

inhibitin gthe activity of the encoded gene
product would serve to inhibit tumor cell angiogenesis. Detection of expression of these sequences

in **colon** cancer tissue can be valuable in determining diagnostic, prognostic and/or treatment information associated with the prevention of achieving the malignant state. . .

--- - - - -------

I 5

Example 8: High Metastatic Potential **Colon** Cancer Versus Low Metastatic **Colon** Cancer Cells

Table 8 summarizes polynucleotides that represent genes differentially expressed between high metastatic potential and low metastatic potential **colon** cancer cells.

Table 8. Low metastatic potential **colon** (lib2) > high metastatic potential **colon** cancer cells (lib I)

SEQ ED NO: ILibl Clones ILib2CIones ILib2/Libl I

157 8 i 8.67

--- -------

1103 i 0 6 16.5

16.5

i 189]o

Example 9: High Tumor Potential **Colon** Tissue Vs. Metastasized **Colon** Cancer Tissue

The following table summarizes polynucleotides that represent genes differentially expressed between high tumor potential **colon** cancer cels and cells derived from high metastatic potential **colon** cancer cells of a patient.

Table 9. High tumor potential **colon** tissue (lib 1 6) vs. high metastatic **colon** tissue (lib 1 7)

SEQ ED NO: I Lib 16 Clones Lib 17 Clones ILibl

100 io 6.89

I 3 112

370 3.94

....

134 Low Met **Colon** (lib2) > High Met **Colon** (lib 1) 67

134 High Met Breast (lib3) > Low Met Breast (Lib4) 85

1209 Low Met Lung (lib9) > High Met Lung (lib8) 17.44

1209 '**Colon** Tumor Tissue (libl6) > Normal **Colon** Tissue (libI 5) 3.42

209 **Colon** Tumor Tissue (lib 19) > Normal **Colon** Tissue (lib 1 8) 5

209 High Met **Colon** Tissue (lib20) > Normal **Colon** Tissue (lib 1 8)

1209 **Colon** Tumor Tissue (lib I 9) > High Met **Colon** Tissue (lib20) 74

1316 High Met **Colon** (lib 1) > Low Met **Colon** (lib2) 15.76

i316 Low Met Breast (lib4) > High Met Breast (Lib3) 17.28

645 Low Met Breast (lib4) > High Met Breast. . .

toward a metastatic phenotype. For example, SEQ ID NO:209 corresponds to a gene that is expressed at relatively higher levels in **colon** tumor tissue than in high metastatic potential **colon** tumor tissue, and at relatively higher levels in high metastatic potential **colon** tumor tissue than in normal **colon** tissue. Thus a relatively increased level of expression of the gene corresponding to SEQ ID NO:209 may be used as marker of a pre-metastatic **colon** cells either alone

or in combination with other markers.

genome IE-35
490 JABO16492.1 Homo sapiens hJTB gene, complete cds e-I 18
491 X98176 H.sapiens mRNA for MACH-beta- I protein IE-36
Homo sapiens **huntingtin interacting protein**
HYPK mRNA,
492 AF049613 partial cds 7E-22
493 AF039690.1,HomosapiensantigenNY-CO-8(NY-CO-8)mRNA,partialeds IE-37
INM-001003IHomo sapiens ribosomal protein, large, PI ribosomal
494 phosphoprotein PI mRNA, complete cds. 4E-3.

WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Wednesday, July 20, 2005

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT,EPAB; PLUR=YES; OP=OR	
☐	L34	l27 and probe	1
☐	L33	l27 and complementary	0
☐	L32	6316272.pn.	1
☐	L31	L30 not @ay>2001	19
☐	L30	l1 and (prostate or colon)	33
☐	L29	L28 not @ay>2001	19
☐	L28	l3 and (prostate or colon)	33
☐	L27	6794501.pn.	1
☐	L26	6794501.pn	0
☐	L25	L24 and l1	0
☐	L24	colorectal.ti.	198
☐	L23	L22 and (prostate or colon)	0
☐	L22	6235879.pn.	1
☐	L21	L20 and L14	2
☐	L20	L19 and L12	3
☐	L19	(ross or mizukami or Rao).in.	20409
☐	L18	L2 and L12	5
☐	L17	L13 and (prostate or colon)	2
☐	L16	L15 and (prostate or colon)	2
☐	L15	L13 and L14	2
☐	L14	L2.clm.	34430
☐	L13	L3 and L12	5
☐	L12	L7 or L8 or L10	7
☐	L11	L7 or L8 or L10L10	4
☐	L10	L1.ab.	6
☐	L9	L1.ab. L8	7
☐	L8	L1.ti.	3
☐	L7	L1.clm.	3
☐	L6	L5 and (screen$ or detect$ or determin$ or diagnos$)	30
☐	L5	L3 and L4	30
☐	L4	= 2001	5469895

☐	L3	L1 and L2	58
☐	L2	cancer$ or neoplas$ or angiogen$ or tumor$	170265
☐	L1	hip1 or (huntington adj interacting adj protein)	69

END OF SEARCH HISTORY

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 FILE 'CANCERLIT' ENTERED AT 08:12:12 ON 20 JUL 2005
L1           29 S HIP1 OR (HUNTINGTIN () INTERACTING PROTEIN)
L2      1221530 S CANCER? OR TUMOR? OR NEOPLAS?
L3        44388 S PROSTAT OR COLON
L4       158156 S PROSTAT? OR COLON?
L5            3 S L4 AND L1

     FILE 'MEDLINE' ENTERED AT 08:14:55 ON 20 JUL 2005
L6          124 S HIP1 OR (HUNTINGTIN () INTERACTING PROTEIN)
L7      1726468 S CANCER? OR TUMOR? OR NEOPLAS?
L8       161221 S PROSTATE OR COLON
L9            3 S L8 AND L6

     FILE 'CAPLUS' ENTERED AT 08:15:52 ON 20 JUL 2005
L10         176 S HIP1 OR (HUNTINGTIN () INTERACTING PROTEIN)
L11       89631 S PROSTATE OR COLON
L12          17 S L10 AND L11
L13     2474250 S SCREEN? OR IDENTIF? OR DETECT?
L14     1134526 S EXPRESS?
L15          15 S L14 AND L12
L16          12 S L15 AND L13
L17           0 S L16 NOT PY>2001
L18           0 S L17 NOT PY>2002
L19           0 S L16 NOT PY>2002

     FILE 'PCTFULL' ENTERED AT 08:18:19 ON 20 JUL 2005
L20         122 S HIP1 OR (HUNTINGTIN () INTERACTING PROTEIN)
L21       34409 S PROSTATE OR COLON
L22       87552 S CANCER? OR TUMOR? OR NEOPLAS?
L23         113 S L22 AND L20
L24          79 S L23 AND L21
L25           7 S L24 NOT PY>2000
L26          80 S L20 AND L21
L27           7 S L26 NOT PY>2000
L28      386911 S SCREEN? OR DETECT? OR DIAGNOS?
L29          79 S L28 AND L26
L30           5 S L20/AB
L31           1 S L30 AND L21
L32          14 S L20/CLM
L33           7 S L32 AND L21
L34           7 S L33 AND L28
L35           3 S L34 NOT PY>2001
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